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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,344	06/25/2003	Tuo Jin	692-A-US	3985

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EXAMINER
ALSTRUM ACEVEDO, JAMES HENRY

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 09/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/606,344	JIN, TUO	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/10/2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 16-19* is/are rejected.

7)☒ Claim(s) *2,5,7,10 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/6/03;12/22/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-19 are pending. Receipt and consideration of Applicant's IDS's (submitted on 10/6/03 & 12/22/03), response to the restriction requirement, arguments/remarks, amended claims, submitted on July 10, 2006 and is acknowledged. Claims 1-13 and 16-19 are under consideration in the instant office action.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-13 and 16-19) in the reply filed on July 10, 2006 is acknowledged. The traversal is on the ground(s) that July 10, 2006. This is not found persuasive because a search of the composition will not necessarily uncover the claimed method of making said composition, which can be made by a different method as described in the restriction requirement mailed on June 14, 2006. Therefore, a second search would be required to evaluate the patentability of the non-elected invention.

The requirement is still deemed proper and is therefore made FINAL.

Claims 14-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on July 10, 2006.

Information Disclosure Statement

The IDS's submitted on 10/6/03 and 12/22/03 have been considered.

It is noted that the references cited in the Search Report PCT/CN03/00492 have been considered. Applicant did not provide foreign reference, WO 01/32139, and neither reference cited in the international search report was listed on a PTO-892.

Specification

The disclosure is objected to because of the following informalities: the word "phospholipid" on page 8, line 16 is spelled with an unnecessary hyphen as "phospho-lipid" and the word "triamterene" is misspelled on the 1st line of Example 4 as "triamteren."

Appropriate correction is required.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claims 2, 5, 7, 10, and 11 are objected to because of the following informalities: (1) a comma should be inserted in claim 2, line 6 after the word "microemulsion;" (2) on line 2 of claim 5 it appears that either the word "said" or the article "the" is erroneously present; (3) the words "gelucire" and "bay" in claim 7 are not proper nouns and should not be capitalized; (4) claim 10, line 3 has an unnecessary right parentheses after "nm" and before the period; and (5) claim 11 does not end in a period or any punctuation, for that matter. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is vague and indefinite because it recites "cellulose derivatives," which is not defined in the specification. It would be unclear to a person of ordinary skill in the art what are the intended metes and bounds of the term "cellulose derivative," because said term is undefined and could refer to such disparate species as esterified cellulose to a single carbon atom, which once was part of cellulose.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-9, 12-13, and 16-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Pather et al. (U.S. Patent No. 6,280,770; IDS reference) as evidenced by K.

Y. Yang et al. ("Effects of Amorphous Silicon Dioxides on Drug Dissolution," *Journal of Pharmaceutical Sciences*, 1979, *68(5)*, 560-565).

Applicant claims a free-flowing compressible composition that facilitates dissolution and water dispersion of poorly soluble or insoluble compounds (claim 1) comprising a solid lipid or solid lipid mixture that dissolves water-insoluble or poorly soluble compounds, is absorbable in a melt state by a porous powder or a mixture of porous powders, and forms solutions, micelles, a microemulsion, or an emulsion in an aqueous medium (claim 2) or also comprising porous powder or a mixture of porous powders (claim 3), and a compound that dissolves in the lipid (claim 4), wherein the lipids are amphiphilic compounds (claim 6), such as gelucire, vitamin E TPGS, bay 10, fatty acids, phospholipids, or non-phospholipids (claim 7). The porous powders having sufficient specific surface area (i.e. greater than 100 m^2/g) (claims 8-9) and pore structure (i.e. pore diameters less than 50 nm) and the porous powders are alumina, silica, or cellulose derivatives (claim 11). The lipid soluble, water insoluble, or poor water-soluble compound is cyclosporine, triamterene, acyclovir, doxorubicin, labetalol, doxepin, methyldopa, or pentoxifyll (claim 12) and the composition is a pharmaceutical composition comprising a pharmaceutically acceptable carrier (claim 13). Claims 16-19 are product-by-process claims wherein the process is as described in claim 14 and the product is the composition of claim 2 (claim 16); a pharmaceutical composition comprising the composition of claim 16 (claim 17), the composition of claim 16 formulated in powders, capsules, granules, and coated variants thereof (claim 18); and the formulation of claim 18 comprising excipients selected from the group consisting of binders, diluents, disintegrants, coating material, and lubricants (claim 19).

NOTE: (1) Claims 14-15 are not under consideration in the instant office action and were not examined. (2) Claims 16-19 are product-by-process claims. Process steps that do not modify the structural characteristics of the instant products are given no weight, as the case for claims 16-19 of the instant application (MPEP §2113).

Pather discloses microemulsion as solid dosage forms for oral administration comprising drug-containing microemulsions absorbed onto solid particles, which may be further formulated into solid dosage forms, and improve the bioavailability of a wide range of drugs (title, abstract, Fig. 1). Microemulsions are pharmaceutically acceptable carriers. The bioavailability of a drug (i.e. its absorption after administration) is attributed to two processes: (1) dissolution of the drug in physiological fluids and (2) the absorption process itself (col. 1, lines 34-37). Specifically, Pather discloses pharmaceutical carrier microemulsions, which are absorbed onto solid particulate absorbents (col. 4, lines 25-29), which can be combined with additional excipients and made into other solid dosage forms, including **tablets, granules, pellets, or other multiparticulate, capsules, and free-flowing powders** (col. 6, lines 8-10, 64-67; col. 9, lines 23-33 [tablets], 34-48 [coated tablets], 49-56 [pellets], 58-67 and col. 10, lines 1-2 [granules]; Examples 1-4, claims 10-16). In Pather's compositions, the drugs are maintained in a microemulsion in vivo, which thereby **enhances dissolution** (col. 3, lines 12-18 and 22-25).

Pather discloses that any non-toxic oil may be used including, **mono-, di-, and triglycerides, *fatty acids* and their esters**, esters of propylene glycols or other polyols, natural oils, such as cottonseed oil, soybean oil, sunflower oil, canola oil, etc. (col. 5, lines 35-43). Any non-toxic surfactant may be used in the microemulsion including various grades of commercial

products: TWEENS® (polyethylene glycol sorbitan laurates), ARLACEL® (dianhydro-d-mannitol monooleate), CAPMUL® (mono-and diglycerides of glycerine and specific fatty acids), MIGLYOL® (coconut oil triglycerides), etc. (col. 5, lines 35-44). The non-toxic absorbent is preferably a fine particulate, including clays, **silicon dioxide (i.e. silica),** wherein silica is preferred (col. 5, line 66 though col. 6, line 7; claim 6). Examples of drugs suitable for incorporation into Pather's invented compositions include **acyclovir, doxepin, doxorubicin, labetalol, methyldopa, nalbuphine, pentoxifyll, and cyclosporin** (col. 6, lines 57-63; claim 10). Examples of filler excipients (i.e. diluents) that can be used to make a tablet from Pather's compositions include mannitol, dextrose, sucrose, and calcium carbonate (col. 9, lines 42-43).

Pather lacks the express disclosure that the invented compositions are capable of absorbing a lipid in the melt state. It is the Examiner's position that this property is inherent to silicon dioxide (i.e. silica), because this is the same material claimed by Applicant as having said material. Because Pather's compositions comprise silica as an absorbent material these compositions inherently have the property of absorbing a lipid in the melt state. Dependent claims 2, 3, 8, and 9 require that the powders used are porous and have a surface area greater than 100 m^2/g. It is Examiner's position that the silica used by Pather is inherently porous and has a surface area greater than 100 m^2/g as evidenced by Table I in Yang et al. (pg. 561) where it is demonstrated that several commercially available amorphous silicon dioxides (i.e. silicas) all have surface areas of 290 m^2/g or more; and porous structures, as evidenced by the fact that all three silicas in Table I have measurable average pore diameters.

Claims 1, 3, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by A. Sheth et al. ("Use of Powdered Solutions to Improve the Dissolution Rate of Polythiazide Tablets," *Drug Development and Industrial Pharmacy*, 1990, *16(5)*, 769-777 [IDS reference]) as evidenced by K. Y. Yang et al. ("Effects of Amorphous Silicon Dioxides on Drug Dissolution," *Journal of Pharmaceutical Sciences*, 1979, *68(5)*, 560-565).

Applicant's claims have been described above.

Sheth discloses **free-flowing powder (i.e. granular) compositions compressed into tablet formulations** by direct compression and comprising solutions of polythiazide (a drug) in polyethylene glycol 400 in admixture with microcrystalline **cellulose** (RC-591), wherein the **dissolution rate of polythiazide from these tablets was significantly more rapid than from commercially available tablets**. Sheth concluded that the dissolution rate of sparingly soluble, hydrophobic drugs can be markedly improved by incorporation of powdered solution into tablets (conclusion #1) (abstract; "Preparation of Powdered Solution of Polythiazide" pg. 771-772; "Preparation of Tablets" on page 772; Figure. 1 on pg. 774 and paragraph on said page; conclusions on pg. 776-777).

Claims 1, 3, and 8-11 are rejected under 35 U.S.C. 102(b) as being anticipated by K. Y. Yang et al. ("Effects of Amorphous Silicon Dioxides on Drug Dissolution," *Journal of Pharmaceutical Sciences*, 1979, *68(5)*, 560-565).

Applicant's claims have been described above.

Yang discloses the effects of amorphous silicon dioxides (i.e. silicas) on drug dissolution (title, abstract, Fig. 1, Fig. 2, Tables III-VI, Fig. 4). In most of the samples studied the

incorporation of amorphous silica greatly enhanced the amount of drug dissolved, regardless of the silica sample used, with the exception of prednisone-silica 63 depicted in Fig. 2. The drugs studied were digoxin, griseofulvin, and prednisone, which are hydrophobic drugs that are either water insoluble or poorly water-soluble.

Yang (pg. 561) demonstrated that the commercially available amorphous silicon dioxides (i.e. silicas) used in the study all have surface areas of 290 m^2/g or more; and porous structures, as evidenced by the fact that all three silicas in Table I have measurable average pore diameters. Silica 63, silica 72, and silica 266 have pore diameters of 20 Å, 150 Å, and 210 Å, which meets the limitation of claim 10 for all silicas used by Yang (1 Å = 0.1 nm).

Other Matter

It appears there is an inadvertent page break in the specification between the "Background" and "Summary" sections. The Examiner respectfully suggests removal of the unnecessary page break. It appears that the compound "pentoxifyll" in claim 12 is misspelled as "pentoxifill." The Examiner respectfully suggests correction of the spelling mistake.

Conclusion

Claims 1-13 and 16-19 are rejected. Claims 2, 5, 7, 10, and 11 are objected. No claims under consideration in the instant office action are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571)

272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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